



Scientific Opinion on the substantiation of a health claim related to an equimolar mixture of the CLA isomers c9,t11 and t10,c12 (marketed as Clarinol® and Tonalin®) and “contributes to a reduction in body fat mass” pursuant to Article 13(5) of Regulation

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SCIENTIFIC OPINION

Scientific Opinion on the substantiation of a health claim related to an equimolar mixture of the CLA isomers *c9,t11* and *t10,c12* (marketed as Clarinol[®] and Tonalin[®]) and “contributes to a reduction in body fat mass” pursuant to Article 13(5) of Regulation (EC) No 1924/2006¹

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)^{2,3}

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

Following an application from BASF SE and Stepan Lipid Nutrition, submitted for the authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of the Netherlands, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to an equimolar mixture (marketed under the trade names Clarinol[®] and Tonalin[®]) of the two conjugated linoleic acid (CLA) isomers *c9,t11* and *t10,c12*. The Panel considers that the food is sufficiently characterised. The claimed effect is “contributes to a reduction in body fat mass”. In previous assessments on the safety of these equimolar isomeric mixtures of CLA, the NDA Panel considered that the observed increase in plasma and urinary concentrations of isoprostanes, which may indicate an increase in lipid peroxidation, and the increase in some markers of subclinical inflammation associated with CLA consumption, together with the limited data available on the effects of CLA on vascular function, may indicate a potential for vascular damage in the longer term. The Panel considers that the information provided does not establish that a reduction in body fat mass, when accompanied by an increase in markers of lipid peroxidation and inflammation, is a beneficial physiological effect for the target population. The Panel concludes that a cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c9,t11* and *t10,c12*, marketed under the trade names of Clarinol[®] and Tonalin[®], and a beneficial physiological effect.

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KEY WORDS

CLA, conjugated linoleic acid, Clarinol[®], Tonalin[®], body fat mass, health claims

¹ On request from the Competent Authority of the Netherlands following an application by BASF SE and Stepan Lipid Nutrition, Question No EFSA-Q-2014-00580, adopted on 11 December 2014.

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SUMMARY

Following an application from BASF SE and Stepan Lipid Nutrition, submitted for the authorisation of a health claim pursuant to Article 13(5) of Regulation (EC) No 1924/2006 via the Competent Authority of the Netherlands, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver an opinion on the scientific substantiation of a health claim related to an equimolar mixture (marketed under the trade names of Clarinol[®] and Tonalin[®]) of the two conjugated linoleic acid (CLA) isomers *c9,t11* and *t10,c12*, and “contributes to a reduction in body fat mass”.

The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence.

The food that is the subject of the health claim is Clarinol[®] or Tonalin[®], which provide a minimum of 78 % of total fatty acids as CLA and a minimum of 74 % of total fatty acids as the two CLA isomers *cis-9,trans-11* (*c9,t11*) and *trans-10,cis-12* (*t10,c12*) at an equimolar (1:1) ratio. The Panel considers that the food, an equimolar mixture of the CLA isomers *c9,t11* and *t10,c12*, marketed under the trade names of Clarinol[®] and Tonalin[®], is sufficiently characterised.

The claimed effect is “contributes to a reduction in body fat mass”. The target population proposed by the applicant is “healthy overweight or class I obese male and female adults, either sedentary or physically active, who wish to reduce their body fat mass”. The Panel notes that an excess of body fat, and in particular of abdominal fat, is associated with adverse health effects, e.g. impaired glucose tolerance, dyslipidaemia and high blood pressure. The Panel also notes that a reduction of body fat through energy (i.e. caloric) restriction and/or through an increase in energy expenditure (i.e. physical exercise/activity) is generally accompanied by an improvement of such adverse health effects. In this context, the Panel considers that a reduction of body fat, with or without a reduction of body weight, is a beneficial physiological effect for overweight subjects in the general population.

In previous assessments on the safety of these equimolar isomeric mixtures (*c9,t11* and *t10,c12*) of CLA (marketed as Clarinol[®] and Tonalin[®]), the NDA Panel considered that the observed increase in plasma and urinary concentrations of isoprostanes, which may indicate an increase in lipid peroxidation, and the increase in some markers of subclinical inflammation (i.e. 15-*keto*-dihydroprostaglandin F_{2α} and possibly C-reactive protein) associated with CLA consumption, together with the limited data available on the effects of CLA on vascular function, may indicate a potential for vascular damage (i.e. atherosclerosis) in the longer term.

In this context, the applicant was requested to clarify how a reduction in body fat mass, when accompanied by an increase in markers of lipid peroxidation and subclinical inflammation, could be considered a beneficial physiological effect for the target population. In reply, the applicant argued that “Clarinol[®] and Tonalin[®] are intended to be used for a period of 6 months to achieve the claimed effect, and that within this dosing duration, there are no adverse effects on insulin sensitivity/glucose metabolism, blood lipids, lipid peroxidation, or subclinical inflammation within the target population (i.e. otherwise healthy overweight or class I obese adults)”.

The Panel notes that, although consumption of the equimolar isomeric mixture of CLA for six months was considered safe for normal-weight, overweight and obese non-diabetic subjects, an increase in lipid peroxidation and in markers of inflammation was observed within a time frame of six months. The Panel also notes that the applicant did not provide evidence or a rationale for how a reduction in body fat mass, when accompanied by an increase in markers of lipid peroxidation and inflammation, could be considered a beneficial physiological effect for the target population.

The Panel considers that the information provided by the applicant does not establish that a reduction in body fat mass, when accompanied by an increase in markers of lipid peroxidation and inflammation, is a beneficial physiological effect for the target population.

The Panel concludes that a cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c9,t11* and *t10,c12*, marketed under the trade names of Clarinol[®] and Tonalin[®], and a beneficial physiological effect.

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BACKGROUND

Regulation (EC) No 1924/2006⁴ harmonises the provisions that relate to nutrition and health claims, and establishes rules governing the Community authorisation of health claims made on foods. As a rule, health claims are prohibited unless they comply with the general and specific requirements of this Regulation, are authorised in accordance with this Regulation, and are included in the lists of authorised claims provided for in Articles 13 and 14 thereof. In particular, Article 13(5) of this Regulation lays down provisions for the addition of claims (other than those referring to the reduction of disease risk and to children's development and health) which are based on newly developed scientific evidence, or which include a request for the protection of proprietary data, to the Community list of permitted claims referred to in Article 13(3).

According to Article 18 of this Regulation, an application for inclusion in the Community list of permitted claims referred to in Article 13(3) shall be submitted by the applicant to the national competent authority of a Member State, which will make the application and any supplementary information supplied by the applicant available to the European Food Safety Authority (EFSA).

STEPS TAKEN BY EFSA

- The application was received on 19/08/2014.
- The scope of the application was proposed to fall under a health claim based on newly developed scientific evidence.
- On 12/09/2014, during the validation process of the application, EFSA sent a request to the applicant to provide clarification.
- On 17/09/2014, EFSA received the clarification as submitted by the applicant.
- The scientific evaluation procedure started on 17/09/2014.
- On 16/10/2014, the Working Group on Claims of the NDA Panel agreed on a list of questions for the applicant to provide additional information to accompany the application and the clock was stopped on 27/10/2014, in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
- On 07/11/2014, EFSA received the applicant's reply and the clock was restarted (on 10/11/2014), in compliance with Article 18(3) of Regulation (EC) No 1924/2006.
- During its meeting on 11/12/2014, the NDA Panel, having evaluated the data submitted, adopted an opinion on the scientific substantiation of a health claim related to an equimolar mixture (marketed as Clarinol[®] and Tonalin[®]) of the CLA isomers *c9,t11* and *t10,c12* and "contributes to a reduction in body fat mass".

TERMS OF REFERENCE

EFSA is requested to evaluate the scientific data submitted by the applicant in accordance with Article 16(3) of Regulation (EC) No 1924/2006. On the basis of that evaluation, EFSA will issue an opinion on the scientific substantiation of a health claim related to: an equimolar mixture (marketed under the trade names of Clarinol[®] and Tonalin[®]) of the CLA isomers *c9,t11* and *t10,c12* and "contributes to a reduction in body fat mass".

⁴ Regulation (EC) No 1924/2006 of the European Parliament and of the Council of 20 December 2006 on nutrition and health claims made on foods. OJ L 404, 30.12.2006, p. 9–25.

EFSA DISCLAIMER

The present opinion does not constitute, and cannot be construed as, an authorisation for the marketing of an equimolar mixture of the CLA isomers *c9,t11* and *t10,c12*, a positive assessment of its safety, nor a decision on whether an equimolar mixture of the CLA isomers *c9,t11* and *t10,c12* is, or is not, classified as a foodstuff. It should be noted that such an assessment is not foreseen in the framework of Regulation (EC) No 1924/2006.

It should also be highlighted that the scope, the proposed wording of the claim, and the conditions of use as proposed by the applicant may be subject to changes, pending the outcome of the authorisation procedure foreseen in Article 18(4) of Regulation (EC) No 1924/2006.

INFORMATION PROVIDED BY THE APPLICANT

Applicants' name and address

BASF BE, Global Segment Management/Human Nutrition, ENS/H, Carl Bosch Strasse 38, 67056 Ludwigshafen, Germany.

Stepan Lipid Nutrition, Museumlaan 16, 1541 LP Koog aan de Zaan, The Netherlands.

Food/constituent as stated by the applicant

According to the applicant, the food that is the subject of the health claim is Clarinol[®] or Tonalin[®], which provide a minimum of 78 % of total fatty acids as conjugated linoleic acid (CLA) and a minimum of 74 % of total fatty acids as the two CLA isomers *c9,t11* and *t10,c12* at a ratio of 50:50, in either triacylglycerol or free fatty acid form.

Health relationship as claimed by the applicant

According to the applicant, the consumption of Clarinol[®] or Tonalin[®] contributes to a reduction in body fat mass.

In relation to the proposed mechanism by which the food would exert the claimed effect, the applicant claimed that Clarinol[®] or Tonalin[®] increase lipolysis and the beta-oxidation of fatty acids, as well as energy expenditure and metabolic rate. The proposed underlying mechanism is that the CLA isomers in Clarinol[®] or Tonalin[®] act as peroxisome proliferator-activated receptor (PPAR)- γ antagonists (Kennedy et al., 2008), which would lead to the activation of adenosine monophosphate-activated protein kinase (AMPK) (Jiang et al., 2012). The activation of AMPK increases the rate of lipolysis and upregulates uncoupling proteins (UCPs), which use energy sources to generate heat (Evans et al., 2002; Zhai et al., 2010).

Wording of the health claim as proposed by the applicant

The applicant has proposed the following wording for the health claim: "Consumption of Clarinol[®] or Tonalin[®] contributes to a reduction in body fat mass".

Specific conditions of use as proposed by the applicant

The applicant has proposed an intake of 4.0 to 4.5 g Clarinol[®] or Tonalin[®] per day. According to the applicant, this amount can reasonably be consumed as part of a balanced diet. The duration required to see an effect should be set at six months.

The target population proposed by the applicant is healthy overweight or class I obese male and female adults, either sedentary or physically active, who wish to reduce their body fat mass.

ASSESSMENT

1. Characterisation of the food/constituent

The food that is the subject of the health claim is Clarinol[®] or Tonalin[®], which are oils rich in conjugated linoleic acid (CLA).

CLA refers to a group of positional and geometric isomers of linoleic acid that are characterised by the presence of conjugated dienes. CLA is a natural, but minor, component of fats from ruminant

animals and is present in the human diet primarily in meat and dairy products. In nature, the most abundant isomer is *cis*-9,*trans*-11 (*c9,t11*).

Clarinol[®] or Tonalin[®] provide a minimum of 78 % of total fatty acids as CLA and a minimum of 74 % of total fatty acids as the two CLA isomers *c9,t11* and *trans*-10,*cis*-12 (*t10,c12*), which are present at an equimolar (1:1) ratio. These isoforms can be measured in foods by established methods. Clarinol[®] and Tonalin[®] have been characterised (EFSA NDA Panel, 2010a, b).

An overview of the manufacturing process, batch-to-batch variability and information regarding stability of the oils were provided.

The Panel considers that the food, an equimolar mixture of the two CLA isomers *c9,t11* and *t10,c12*, marketed under the trade names of Clarinol[®] and Tonalin[®], which is the subject of the health claim, is sufficiently characterised.

2. Relevance of the claimed effect to human health

The claimed effect proposed by the applicant is “contributes to a reduction in body fat mass”. The target population proposed by the applicant is “healthy overweight or class I obese male and female adults, either sedentary or physically active, who wish to reduce their body fat mass”.

The Panel notes that an excess of body fat, and in particular of abdominal fat, is associated with adverse health effects, e.g. impaired glucose tolerance, dyslipidaemia and high blood pressure. The Panel also notes that a reduction of body fat through energy (i.e. caloric) restriction and/or through an increase in energy expenditure (i.e. physical exercise/activity) is generally accompanied by an improvement of such adverse health effects. In this context, the Panel considers that a reduction of body fat, with or without a reduction of body weight, is a beneficial physiological effect for overweight subjects in the general population.

In previous assessments on the safety of an equimolar isomer mixture (*c9,t11* and *t10,c12*) of CLA (marketed as Clarinol[®] and Tonalin[®]) as a Novel Food ingredient (EFSA NDA Panel, 2010a, b, 2012), the NDA Panel considered that “the administration of the 1:1 isomer mixture of CLA to normal-weight, overweight and obese non-diabetic subjects does not appear to have adverse effects on insulin sensitivity, blood glucose control or liver function at the proposed conditions of use up to six months. [...] However, the observed increase in plasma and urinary concentrations of isoprostanes, which may indicate an increase in lipid peroxidation, and the increase in some markers of subclinical inflammation (i.e. 15-*keto*-dihydroprostaglandin F_{2α} and possibly C-reactive protein) associated with CLA consumption, together with the limited data available on the effects of CLA on vascular function, may indicate a potential for vascular damage (i.e. atherosclerosis) in the longer term”.

In this context, the applicant was requested to clarify how a reduction in body fat mass, when accompanied by an increase in markers of lipid peroxidation and subclinical inflammation, could be considered a beneficial physiological effect for the target population. In reply, the applicant argued that “Clarinol[®] and Tonalin[®] are intended to be used for a period of 6 months to achieve the claimed effect, and that within this dosing duration, there are no adverse effects on insulin sensitivity/glucose metabolism, blood lipids, lipid peroxidation, or subclinical inflammation within the target population (i.e. otherwise healthy overweight or class I obese adults)”.

The Panel notes that, although consumption of the equimolar isomeric mixture of CLA for six months was considered safe for normal-weight, overweight and obese non-diabetic subjects, an increase in lipid peroxidation and in markers of inflammation was observed within a time frame of six months. The Panel also notes that the applicant did not provide evidence or a rationale for how a reduction in body fat mass, when accompanied by an increase in markers of lipid peroxidation and inflammation, could be considered a beneficial physiological effect for the target population.

The Panel considers that the information provided by the applicant does not establish that a reduction in body fat mass, when accompanied by an increase in markers of lipid peroxidation and inflammation, is a beneficial physiological effect for the target population.

The Panel concludes that a cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c9,t11* and *t10,c12*, marketed under the trade names of Clarinol® and Tonalin®, and a beneficial physiological effect.

CONCLUSIONS

On the basis of the data presented, the Panel concludes that:

- The food, an equimolar mixture of the CLA isomers *c9,t11* and *t10,c12*, marketed under the trade names of Clarinol® and Tonalin®, which is the subject of the health claim, is sufficiently characterised.
- The claimed effect proposed by the applicant is “contributes to a reduction in body fat mass”. The target population proposed by the applicant is “healthy overweight or class I obese male and female adults, either sedentary or physically active, who wish to reduce their body fat mass”. The information provided by the applicant does not establish that a reduction in body fat mass, when accompanied by an increase in markers of lipid peroxidation and inflammation, is a beneficial physiological effect for the target population.
- A cause and effect relationship has not been established between the consumption of an equimolar mixture of the CLA isomers *c9,t11* and *t10,c12*, marketed under the trade names of Clarinol® and Tonalin®, and a beneficial physiological effect.

DOCUMENTATION PROVIDED TO EFSA

Health claim application on Clarinol® or Tonalin® and contributes to a reduction in body fat mass pursuant to Article 13(5) of Regulation (EC) No 1924/2006 (EFSA-Q-2014-00580, Claim serial No: 0426_NL). August 2014. Submitted by BASF SE and Stepan Lipid Nutrition.

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ABBREVIATIONS

CLA conjugated linoleic acid

c9,t11 *cis-9,trans-11*

t10,c12 *trans-10,cis-12*